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It is, of course, desirable that similar scales be worked out for as many different sections of the population as possible; but, to most private investigators, the cost of collecting data for derivation of such scales is prohibitive. The belief is ventured that, in most cases, such a special study is not essential, as the scales here presented probably will not give rise to serious errors when applied to other sections of the population—especially to other wage-earning groups. It is practically certain that results derived by the use of these scales would, at least, be decidedly superior to those obtained by classifying families on the basis of net income for the family as a whole, without considering its size and composition, or even by figuring the net per capita income for each family.

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## ONE OR SEVERAL SPECIES OF MALARIA PARASITES?

### A REVIEW OF RECENT WORK BEARING ON THIS QUESTION.

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The treatment of malarial fevers has been based partially on the classification of the types of the disease. The intelligent physician varies the specific treatment on the basis of microscopical findings and clinical symptoms. Therefore, the aid of the microscope must be sought in making a final decision. The differentiation of the various types of malaria plasmodia has been assumed by the clinician, the zoologist taking a subordinate part in the decision pertaining thereto. Possibly this may explain the confusion of the status of the parasitology of this disease. It is believed that the question whether the *Plasmodium* of malaria is a plural organism or a single polymorphic organism capable of causing one set of symptoms at one period and a different set of symptoms at another period in its life history is of more than academic interest. Assuming, then, that the problem is of sanitary importance, the matter is here given some consideration.

Although it has been generally accepted that the three species of *Plasmodium*, namely *P. vivax*, *P. falciparum*, and *P. malariae* are distinct, the question of the complete transformation of the parasites of malaria has recently assumed much prominence in the literature of malariology. During the World War this question was given renewed interest through observations made on troops infected in the Balkans and subsequently repatriated. With the notable exception of the opinions of Laveran, the views upholding the unity of the species of *Plasmodium* were for the most part hastily constructed, and the recent additions to the literature give evidence of incomplete observations such as only war conditions could warrant.

Guided by the consensus of opinion of conservative workers in parasitology, it is safe to assume the following as the status of the

question under discussion: Assertions maintaining the unity of the malaria parasites and the transmutation of species can be accounted for by the presence of unrecognized cases of mixed infections.

The following references to the available literature give a historical survey bearing on the problem.

Laveran (1893), who is the strongest advocate of the unity of the malaria parasite, states:

"I arrived, in 1884, at the conclusion that the different forms in which the hæmatozoa of paludism present themselves belong to one and the same polymorphic parasite; since then I have always upheld this opinion.

"Is there but one hæmatozoon of paludism? Is there a single polymorphic parasite, or are there several species of parasites giving rise to different clinical manifestations of paludism?

"The theory of the plurality of the hæmatozoa of paludism raises numerous objections. The unity of paludism, from a clinical and anatomico-pathological point of view, is indisputable. Certain forms under certain conditions are oftener met with, e. g., the tertian and the quartan types are much more common in our climate than in hot countries; but it can not be said that here is a home of tertians, there a home of quartans and irregular fevers; it is in the same endemic centers that fevers of different types are contracted, and these types vary in a regular manner with the season and the climate.

"It is a well-known fact that the fever often changes its type in the same patient; it is rare, especially in hot countries, for a fever to begin with the tertian or quartan type; more generally it is first continued or quotidian, and at the time of a relapse it is transformed into a tertian or a quartan. The type of fever may even modify itself when patients have left the palustral countries under conditions which exclude the idea of a new infection. If these facts are to be explained on the hypothesis of the plurality of parasites, it will be necessary to admit that the different species of hæmatozoa must generally coexist in the same patient and are in turn predominant.

"The crescent-shaped bodies are, it is true, very characteristic, and were it proved that they are always present in the irregular fevers and never in the regular fevers, we might admit the two varieties described by Grassi and Feletti. But the relations which exist between the appearance of crescent-shaped bodies in the blood and this or that type of paludism are far from being so simple. The exceptions to the rule, if there be any rule, are very numerous."

Referring to the etiology of malarial fevers, Scheube (1902) remarks: "The fact also that in epidemics of malaria all forms of the disease occur, lends still more color to Laveran's opinion, whereas the results of experimental inoculatory transmissions favor the views of those who maintain the idea of different species."

Thiroux (1906) supports Laveran's view as to the unity of the malaria parasite. He examined native children in Senegal and found that in the hot weather tropical forms amounted to 98.5 per cent of the whole number examined, and large forms (benign tertian and quartan) to 1.5 per cent, whereas in November and December the respective figures of the positive cases were 73.5 and 26.4 per cent and in March and April they were 64.1 and 35.8 per cent of the positive cases. He considers it difficult to admit a summer and winter malaria due to absolutely different species.

Plehn (1907) records a case of tropical malaria acquired in Togoland which afterwards, in Germany, following treatment, became a double benign tertian. He thinks the probability that the patient had a latent benign tertian is negated by the excessive rarity of such occurrence in the district from which he came. According to Plehn it would seem that a single species of malarial parasite is able to undergo variations according to the different countries and climates in which it develops.

Craig (1909) states: "Laveran and his followers believe that the parasite producing malarial fever is a polymorphic organism, assuming very great differences in morphology under differing conditions of environment, and that, in Laveran's words, 'there does exist a constant relation between the forms under which the hæmatozoa appear in the blood and the clinical manifestations of paludism; one can only say that certain forms of the parasite are more often seen in certain cases, the crescents, for instance, in relapses and malaria cachexia.' Some of Laveran's followers even claim to have observed interchangeability of the various species which have been described, but their observations still await confirmation and the great weight of evidence to-day, both morphological and experimental, is in favor of the existence of several species of malarial plasmodia."

Armand-Delille (1917) is impressed with the fact that among the French troops in Macedonia the predominant malarial infection between the beginning of July and the end of March following was *P. falciparum*, and the predominant infection from April to July was *P. vivax*. In October 95 per cent of all cases of malaria were *P. falciparum*. Beginning with April, 115 out of 116 blood examinations showed only *P. vivax*. Again, at the hospital for malarial patients at Vichy, at the end of June and the beginning of July, he could find only *P. vivax*. After the month of December *P. vivax* was completely substituted for *P. falciparum*. Even in patients who had had pernicious malaria, only parasites of benign tertian could be found.

"How is it," this author asks, "that the parasite usually so resistant to quinine disappears in the spring, giving place then to the parasite usually so sensitive to quinine? Is there a transformation

of *P. falciparum* into *P. vivax*? Is *P. falciparum* merely the form that persists in the internal organs? Is Laveran's theory of the unity of the malaria parasites correct?"

Teichmann (1917) treated 24 cases of tropical malaria for four to five months in a German military hospital in Turkey and found his cases harbored *P. vivax* at the end of the treatment. He states that recent infection was out of the question and rejects all of the usual explanations: inefficient prophylaxis, quinine-fast parasites, low resistance of the patients, and insufficient treatment.

Von Heinrich (1917) in a paper giving statistics of 1,029 cases treated during seven months at the malaria hospital, Sarajevo, records 150 mixed infections. These in most cases were not diagnosed until the latent benign tertian parasites appeared in the spring, which is their optimum period of development, just as autumn is the optimum period for the tropical parasite. He maintains that the two parasites can be coexistent; that each has its own characters; that no transitional forms were seen; therefore that there is no evidence that one changes into the other as has been supposed by Laveran and others. In recording the type of parasite the author emphasizes that dates should always be given.

Forschbach and Pyszkowski (1918) record a change of type of parasite in three out of seven cases of chronic subtertian malaria. In each case small rings and crescents were present at first and persisted during the winter, and then disappeared to be replaced by benign tertian parasites. The authors offer the following explanations: double infection, superinfection with benign tertian following the removal of cases from Macedonia to Breslau, and conversion of subtertian parasites into tertian.

Gros (1918), relative to the unity of the malaria parasites, offers conclusions based on hypothetical grounds, not on experimental research, as follows:

1. There is only one species of malaria parasite.
2. This species assumes different forms according to the climate, season, and the natural reaction of the host.
3. It is transmissible in each of its several forms, clinical and microscopical.

The author asserts that the simultaneous presence of two forms in the host's blood signifies not a mixed infection but the course of transformation of one form into another.

Verzar (1918) made observations on 2,662 patients infected during the autumn in Albania, Montenegro, and Serbia and brought to Hungary for treatment. Here, from November to February the relapses were chiefly subtertian, and beginning with March they were almost exclusively benign tertian. He made special studies on eight cases which originally harbored subtertian and afterwards tertian

parasites. These conditions were reversed in five other cases. The author made 12,978 examinations, noting the simultaneous appearance of both types of parasites only six times.

Worner (1919) cites some facts in favor of the distinctness of the tertian and subtertian parasites. It was observed that among the troops of which he was in charge the period of tertian infection lasted from the end of July to mid-October, and that of subtertian from mid-July to the beginning of December. Blood examinations in all cases were carefully made through three malarial seasons. His conclusions are as follows:

1. Many patients who suffered an attack of tertian in the spring had had in the previous year first tertian and then subtertian.

2. Many patients had had, clinically and microscopically, only subtertian. All of these men had been in the malaria region during the period when tertian predominated.

3. In the instance of the men who were removed into the district between October and early December and suffered from subtertian, tertian fever in the spring was never observed. The author concludes that the two types of parasites, *P. vivax* and *P. falciparum*, are quite distinct.

Seyfarth (1919), discussing the seasonal appearance of the types of malarial fever, concludes that the existence of three well defined species can not be denied, but that under certain conditions, principally climatic, the occurrence of type transitions is observed. As an argument against mixed infections, the author cites 220 cases of subtertian in which evidence of mixed infection was carefully sought in the autumn and winter but not found. However, in the following spring these relapsed with the presence of tertian parasites. When various provocative measures were applied to crescent carriers, tertian parasites were produced. Following this the crescents gradually disappeared. Seyfarth points to the isolated occurrence of cases of quartan and subtertian in places, for instance, in Germany, where tertian is the only form usually found.

Armand-Delille (1919) supports Laveran's belief that there is only one species of malaria *Plasmodium* and that alternation of parasites is a common occurrence. He thinks this alternation of parasites is to be explained in terms of the infecting anophelines. In other words, *P. vivax* is alone present at the beginning of epidemics, whereas *P. falciparum* appears in the blood at a time when reinoculations occur, and starting from the moment when the sporozoites are introduced in an almost continuous manner into the blood, the schizonts are very small and gametocytes assume the form of crescents, well known for their resistant powers. Further, the supposition is advanced that these forms of resistance and this aspect are the result of a modification of the blood serum, the repeated

inoculations of sporozoites favoring the production of antibodies which determine the production of resistant forms of the parasite. When anophelines disappear during the winter months or the patient, being in a healthy country, is no longer exposed to their bites, antibodies cease to be produced or are gradually eliminated, and the formation of crescents terminates. Instead, he concludes, the parasite perpetuates itself by schizogony and produces large spherical gametocytes capable of surviving over a long period, i. e., until the intermediate hosts start breeding out.

Eisner (1919), after several years' experience with malaria in Macedonia, rejects the theory that there is only one species of malarial parasite. He argues that cases of benign tertian occurring in persons who had suffered the previous summer from tropical malaria only, are readily explained when it is remembered that the former infection frequently remains latent for long periods. Quinine prophylaxis is able to keep benign tertian in subjection but often fails to suppress infection with *P. falciparum*. Hence in cases of double infection the latter is first in evidence while the former only appears at a later date. He notes that in Macedonia infection with tropical malaria was acquired late in the summer at a time when quinine prophylaxis had become slack and irregular, so that *P. falciparum* had a better chance of establishing itself than *P. vivax* infection, which occurred earlier at a time when the prophylaxis was carried out.

The author advances the hypothesis that a tropical infection may actually prevent the development of a benign tertian infection, but brings forward no argument in support of the suggestion. He states that the apparent change of type seen in the initial attack may also be observed in the relapses. Here, processes of immunity may play a part; but whatever the cause, the majority of benign tertian relapses occur in the spring, i. e., from March to May, whereas the tropical relapses, after appearing first in the autumn or throughout the winter, again show themselves in the beginning of summer. Hence, according to Eisner, it is easy to understand that the later benign tertian relapses of early summer may, in the same patient, be followed by recurrences of tropical malaria.

There are, however, other facts which the author advances to disprove the unitarian theory, as, for example, the morphological and histological differences in the parasites, the differences in the types of fever they produce, and numerous specific epidemiological and clinical features which distinguish benign tertian from tropical malaria.

Werner (1919) asserts that he does not believe in the unitarian theory of malaria parasitology. According to this writer the phenomena advanced in its favor may be explained in terms of the biological peculiarities of the mosquito vectors.

Plehn (1919) explains the change of type in malaria infection biologically as follows: "The mosquitoes become infected with large parasites (benign tertian) in spring from relapse cases or early primary cases in which the infection has persisted from the previous year. As soon as it is warm enough they transmit the infection to man, who shows the corresponding type of parasite. Later, under the action of summer heat, the parasites in the mosquito assume other characteristics, so that they acquire, in the first place, the property of destroying the red cells before there is time for the large forms to develop in the latter, and secondly, that of producing crescents. With these characteristics the parasites are transferred to man in the height of summer, and the mosquitoes newly infected by him cause the summer epidemic with small parasites. The mosquitoes infected in the summer are presumed to die in late autumn. During the following months the infection in man weakens, probably under the action of the winter climate, which is not favorable to the parasites. In the later relapses, in many cases, the large parasites with rosettes and spherical gametocytes reappear, provided the infection has not been stamped out. These later relapses, with large parasites, furnish the material for the next year, thus restarting the cycle.

"In northern Europe small forms and crescents are usually not seen, because the temperature is too low to allow them to develop in the mosquitoes. Where the new human infections in the North cease at the height of the summer, we may perhaps assume that the temperature during the year in question was not suitable for the development of the sporozoite broods even of the larger forms. It is easy to explain the exclusive occurrence of the small parasites in tropical equatorial countries by the uniformly high temperature at which the mosquitoes live throughout the year. When, however, in the case of relapse after home leave and residence in a cool country or after the infection is weakened through treatment, the large parasites appear even at the equator, one can no longer deny an action on the part of the human organism. How this takes place is not yet clear."

Reitler (1919) records his observations made in a hospital for malaria in Vienna, where 211 patients were held under close observation for a sufficiently long period under conditions such that risk of reinfection could be excluded. He states that in malignant tertian cases there was a rapid fall from a maximum of positive blood findings in January to a minimum in February, with thereafter a slight rise in April. In benign tertian infections the period of greatest freedom from parasites was in February, and the number of positive blood examinations rose steadily until May, in accordance with the well-known fact that benign tertian relapses are chiefly



seen in the spring. Mixed cases showed an almost constant fall in the number of tropical parasites as contrasted with a constant rise in the number of *P. vivax* infections, the maximum of mixed findings being in March and April. Here again the chief parasite-free period was February.

Reitler states: "This alteration in the parasites seen in the same patient is modified by (1) the provocative influence of high external temperature and strong light, these factors affecting equally both species of parasite; (2) treatment with quinine, *P. vivax* being more susceptible than *P. falciparum*. There are, however, exceptions to the general rule not easily explained. Contrasting the behavior of tropical and tertian parasites in cases of mixed infection, it is seen that temperature and light are not only the factors concerned. The view that tropical infections are less susceptible to these agencies than are benign tertian cases or may even react to them in a different manner is negated by their well-known behavior during the tropical season and by the changes observed by Plehn who, in patients showing only quotidian infections (*P. immaculatum*) in the tropics, found a change of type to *P. vivax* when these patients had returned to Germany. The respective geographical distribution of both species of parasites is also against the hypothesis."

Simons (1919) devotes a portion of his paper to a careful criticism of the unitarian theory. He opposes the hypothesis both on theoretical grounds and from a consideration of the cultural studies. Further, he deals with the question of the influence of temperature on the malarial parasite, a point on which those who hold the unitarian theory lay stress, and cites the work of Sacharoff, who fed a leech on blood containing *P. falciparum*, kept it on ice for four days, injected the blood into himself intravenously, and suffered from a tropical pernicious attack. Simons does not regard this experiment as conclusive evidence, but advances it as an argument against the view that variations in temperature can exercise a profound influence on the form of the *Plasmodium*. He also points out that the unitarian theory, which is concerned with a morphological question, depends chiefly on epidemiological and clinical proofs, not on morphological findings. The evidence he obtained from mixed infections is against the unitarian theory, and he states that in such cases faulty staining technique may lead to fallacious conclusions. In this connection the author recalls his work with trypanosomes and with malaria parasites, more especially crescents, and indicates errors which may arise owing to the inadequate staining when Giemsa's method is employed for thick drop preparations.

#### Recent Experience of the Writer.

Relative to the explanation offered by several workers that the alternation of parasites can be interpreted in terms of the infecting

anophelines, the following account of the writer's experience is submitted. At the outset it is necessary to remind the supporter of the belief in unity of species of plasmodia that if one carefully analyzes the accounts in the literature of approximately 100 mosquito inoculation experiments an incontrovertible fact presents itself. In every instance of positive result the type of parasite imbibed with the blood of the donor was always reproduced with regularity in the volunteer host. One is not prepared to discuss the proportion of cases cited which were mixed infections, as no mention is made of this condition. In this connection it is believed that if suitable mixed infections could be utilized for mosquito infectivity experiments, much could be definitely determined relative to possible change of form in the transference of parasites. A more critical test would thus be established, affording a desirable criterion as to the possibility of reproducing corresponding forms of the parasite from carrier to new host.

In the positive inoculation experiments performed in the Public Health Service malaria laboratory located at Memphis, Tenn., the evidence presented has been uniformly confirmatory of the idea of constancy of species. Sixteen positive experiments are recorded, 2 of them with subtertian malaria and 14 with tertian malaria. The data relative to the reproduction of *P. falciparum* are given herewith.

The blood donor used for the infection of the specimen of *A. quadrimaculatus* was submitted to daily blood examination before and during mosquito biting, showing gametocytes of *P. falciparum* in his blood as tabulated.

TABLE I.—Per cent of subtertian gametocytes in 200-400-leucocyte counts.

Date of experiment.	Per cent of gametocytes.	Date of experiment.	Per cent of gametocytes.
September:		September—Continued.	
1.....	16	12.....	18
2.....	33	13.....	20
3.....	16	14.....	15
4.....	48	15.....	3
5.....	69	16.....	4
6.....	33	17.....	5
7.....	30	18.....	3
8.....	28	19.....	2
9.....	24	20.....	2
10.....	17	21.....	3
11.....	9		

The patient's blood was carefully noted for forms other than crescents, and only an occasional *falciparum* ring was ever seen in the 21 blood examinations.

The mosquito used in this test was applied to a healthy host 15 days following its last infective blood meal. A sharp attack

of subtertian malarial fever followed an incubation period of 11 days, when characteristic ring forms of *P. falciparum* were found in the peripheral blood. Treatment was deferred for three days, during which time the diagnosis was amply substantiated clinically and microscopically. Numerous blood examinations failed to reveal forms other than those typical of subtertian malarial fever, and these were indistinguishable from the young schizonts of *P. falciparum* harbored by the original patient selected to infect the mosquito.

In the second inoculation experiment with subtertian malaria, the blood donor used to infect the specimen of *A. quadrimaculatus* was a typical chronic case of the disease. The blood findings during mosquito biting are noted as follows:

TABLE II.—Per cent of gametocytes in 300-leucocyte counts.

Day of experiment.	Per cent of gametocytes.	Day of experiment.	Per cent of gametocytes.
August:		August—Continued.	
1.....	7	6.....	8
2.....	10	7.....	4
3.....	15	8.....	2
4.....	8	9.....	5
5.....	5		

In addition to the presence of crescents in the patient's blood, there were several days when rings were present in sufficient number to account for the paroxysms that the patient had been observed to suffer. The disease was reproduced in the new host as the result of the mosquito biting, after an incubation period of 12 days, with characteristic symptoms of subtertian malarial fever. In this instance it was not feasible to obtain a blood smear until five days later, when typical ring forms of *P. falciparum* with double chromatin staining bodies were seen.

In the series in which 14 successful inoculations with *P. vivax* resulted, an untreated patient was employed to infect the 3 specimens of *A. punctipennis*. The primary object of the experiment was mosquito infectivity; therefore it was necessary to await gametocyte development, and during this two weeks' interval, daily blood examinations revealed several generations of complete schizogony. The parasites were undoubtedly characteristic forms of *P. vivax*. During the time when the mosquitoes were being applied to the patient, only two days presented suitable conditions for infection. Blood counts at this time revealed an average gametocyte count of 1 to 616 leucocytes. The volunteers used in the biting experiment suffered incubation periods varying from 13 to 19 days; and in each instance the presence of tertian malarial fever was substantially corroborated clinically and microscopically. The parasites observed varied from

young ameboid forms to complete schizogony and gametocyte formation. At least five of the 14 new hosts suffered relapses. The parasites observed on the second series of examinations were constantly and typically *P. vivax*.

The possible relationship of transmutation of malaria species and mixed infections has been brought to our attention in a recent example, the data of which are herewith presented: Five members of a family residing in northeastern Arkansas were found to harbor parasites of malaria during August as follows:

Mr. R., *P. vivax* (rings and gametocytes).

Mrs. R., *P. falciparum* (rings).

B. R., *P. vivax* (rings and gametocytes).

R. R., *P. falciparum* (rings and gametocytes).

A. R., *P. falciparum* (rings and gametocytes).

Two members of this family were selected to provide parasites in mosquito inoculation experiments. These persons were examined daily before and during laboratory experiments at a time when the probability of natural infection could be reasonably excluded. The protocol bearing on these two special cases is given herewith:

*Blood findings in patient R. R.*

Date.	Parasites.	Per cent.
September, 1919:		
2.....	<i>P. falciparum</i> gametocytes.....	2
3.....	do.....	3
4.....	do.....	2
5.....	do.....	1
6.....	do.....	1
8.....	do.....	1
11.....	do.....	.5
18.....	<i>P. vivax</i> rings and young schizonts in large numbers.	

*Blood findings in patient A. R.*

Date.	Parasites.	Per cent.
September, 1919:		
18.....	<i>P. falciparum</i> gametocytes.....	7
19.....	do.....	10
20.....	do.....	15
22.....	do.....	8
23.....	<i>P. falciparum</i> rings and gametocytes.....	5
24.....	<i>P. falciparum</i> gametocytes.....	8
25.....	<i>P. falciparum</i> rings and gametocytes.....	4
26.....	<i>P. falciparum</i> gametocytes.....	2
27.....	do.....	5
November, 1920:		
3.....	<i>P. falciparum</i> rings and few gametocytes.	
26.....	Parasites absent.	
May, 1920:		
28.....	<i>P. vivax</i> gametocytes.....	3
29.....	do.....	2

**Discussion.**

The group of cases presented here is offered as a typical illustration. The writer desires to emphasize that in these mixed infections har-

bored in one household repeated microscopical blood examinations show the relation as indicated in the tables.

The change of findings (from parasites of *P. falciparum* to *P. vivax*) on microscopical examinations was noted during exhaustive tests.

The foregoing data relative to the family R is presented without comment as to the moral indicated. This group and the circumstances involved may be accepted as a typical illustration of what the believer in alternation of parasites offers in support of his claim of transmutation. It is believed that innumerable examples of similar cases can be assembled, and one may draw his conclusions to fit the hypothesis to be defended. The blood samples taken from the cases presented here, though carefully scanned, may or may not have contained more than one type of parasite. Possibly this could not be definitely stated unless spleen or spinal punctures had been made. Again, one can not be certain of fresh infections being due to mosquito biting during the course of observation of these patients, because we do not know to what extent superinfection is a factor. Possible immune bodies produced through the invasion of the first type of parasites may mask the activities of the new species of parasite, inhibiting their development and causing them to remain latent or in retirement in the visceral organs. At any rate, unless more data are contributed through blood cultural studies and mosquito inoculation experiments, I do not believe that one can definitely prove that the plurality of species is not the normal status; and the principle of transmutation remains merely an interesting hypothesis, possibly of equal status with that of parthenogenesis.

*Acknowledgment.*—Acknowledgment is made to the sectional editor on malaria of the *Tropical Diseases Bulletin* for the free use of abstracts.

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## AN OUTBREAK OF BOTULISM AT ST. ANTHONY'S HOSPITAL, OAKLAND, CALIF., IN OCTOBER, 1920.

By J. C. GEIGER, Epidemiologist, United States Public Health Service.

During the month of October, 1920, there occurred in the St. Anthony's Hospital, Oakland, Calif., an outbreak of botulism. There was a total of six cases, two of which could be considered mild and four severe. Of these latter, three died. Unfortunately none of these cases was recognized as botulism until the third day of illness, and therefore they were not immediately reported.